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Adaptive Evolution of Phage Holin Genes: Rapid evolutionary change in transmembrane domains

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Bacteriophages engage in a fierce evolutionary arms race with their host bacteria. The arms race involves many phage proteins associated with distinct phage infection & reproduction steps. By deploying anti-phage countermeasures, bacteria limit the ability of phages to produce progeny phages. Holins are phage proteins that increase the permeability of the cell membranes of the host bacteria and determine the release timing of progeny phages from the bacterial host. While other researchers are characterizing the biology of holin proteins and their role in the lytic cycle, the role of holin mutations in the coevolutionary arms race needs to be better understood. Here, we report the results of the dN/dS adaptive evolution analysis test, allowing us to detect the natural selection activity on a given gene and functional domains within that gene. In a situation in which natural selection is disinterested in the evolution of a given gene, the ratio of the rate of fixation of nonsynonymous mutations (dN) to the rate of fixation of synonymous mutations (dS) is equal to 1; this is the case for pseudogenes. When adaptive selection has occurred, the ratio is greater than 1; this is the case for rapidly evolving genes (or codons within a gene). When purifying selection has occurred, the ratio is less than 1; this is the case for highly conserved genes (or conserved protein active sites within a gene). A high rate of adaptive selection for a given gene (or codon sites within a gene) characterizes the rapid evolutionary change indicative of a coevolutionary arms race between phages and their hosts. A Mixed Effects Model of Evolution (MEME) is a site-by-site dN/dS method available in HyPhy. MEME was used to test 30 putative holin phams. Pham 114820 had the highest proportion of sites under adaptive selection of the tested phams: 8 out of the 14 sites of interest are on the 3 predicted transmembrane domains, while the other 6 sites are predicted to be inside the host cell. Our next step will be to more broadly test phams containing holin or holin-like genes for the signature of adaptive evolution, using the results of this test to characterize the phage-host coevolutionary role of this important gene more fully.